

Original Research Article

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A prospective observational study to describe magnetic resonance imaging findings in perinatal asphyxia in terms of severity, outcome and neurological sequel in term and preterm babies

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ABSTRACT

Background: Perinatal asphyxia is a significant cause of neonatal mortality and morbidity. MRI is useful for assessing the severity and pattern of brain injuries. There is less data of MRI findings of perinatal asphyxia from India and the subcontinents. This prospective observational study was done to describe MRI brain findings in neonates with perinatal asphyxia with respect to various determinants.

Methods: Initial MRI brain was done when babies were stable after fulfilling inclusion criteria. Immediate outcome was assessed at the end of hospital stay. They were followed up for presence of any sequel up to 1 year. Repeat MRI brain was done in few selected babies. Data was collected and statistically analyzed.

Results: Total 55 babies were included in the study (term 27, preterm 28). There were 9 babies in stage I, 17 babies in stage II and 22 babies in stage III. MRI brain findings were normal in 8 and abnormal in 47 patients. There were Deep gray matter injury (DG) in 22, Para Sagittal subcortical white matter injury (PS) in 6, Germinal matrix haemorrhage (GMH), intraventricular haemorrhage (IVH) and Periventricular leucomalacia (PVL) in 12 and Mixed pattern of injury in 7 babies. Findings among 9 expired babies were: 4 (44.4%) DG, 2 (22.2%) GMH+IVH and 3 (33.3%) mixed. There was neurological sequel in 13 babies (48.1%). Babies with normal MRI initially had no sequel.

Conclusion: Brain injury due to perinatal asphyxia follows several patterns according to gestational age and severity. Early and accurate recognition of these patterns with the help of MRI brain helps in managing the baby and predicting the prognosis.

Key word: Gestational age, Hypoxic ischemic encephalopathy, Magnetic resonance imaging brain, Neurological sequel, Perinatal asphyxia

INTRODUCTION

Perinatal asphyxia is a serious condition that causes significant mortality and long-term morbidity. In India, 20% of neonatal death is due to perinatal asphyxia.¹ Apart from mortality, most concerning event of perinatal asphyxia is its neurological sequel.

Various neuroimaging techniques like USG, CT scan, MRI etc. are available for detection of the severity, extent and pattern of brain injuries in HIE and its sequel. Accurate identification and characterization of the severity, extent, and location of brain injury relies on the selection of appropriate neuroimaging modalities. When evaluating CNS injuries in hypoxic neonates, most form of the brain imaging demonstrates evidences

of anatomical alteration of brain including effects of vascular and hypoxic insult.

Cranial USG provides a convenient, noninvasive, relatively low-cost bedside screening examination of the neonate without any radiation exposure, and detect hemorrhage, periventricular leukomalacia (PVL), and hydrocephalus with good sensitivity. But parenchymal abnormalities identified by USG are often nonspecific.² CT is the least sensitive modality for evaluation of HIE because of the high-water content in the neonatal brain and high protein content of the cerebrospinal fluid, which result in poor parenchymal contrast resolution. In addition, CT has the inherent disadvantage of radiation exposure. MRI scan identifies the hypoxic ischemic brain damage in neonate specifically and in early stage. MR has recently been used in some centers to assess brain damage in perinatal and neonatal asphyxia because of its apparent increased sensitivity to structural damage.³⁻⁶ Moreover, MR studies have shown that myelination, a process that cannot be detected by CT, is delayed in patients who suffer perinatal asphyxia.^{7,8} It also helps to exclude other causes of encephalopathy such as hemorrhage, cerebral infarction, neoplasms, or congenital malformations.

There is only a handful of study from India where MRI brain findings were described and also follow up was done. In our study authors have tried to find out the role of MRI in identifying different patterns of injuries in HIE in respect to perinatal brain maturation and the severity of insult. Authors also described association of these findings with disease outcome in terms of mortality and neurological sequel in follow up.

METHODS

The study was conducted in Sick Newborn Care Unit (SNCU) of a tertiary care center of Eastern India. Cases were recruited from January 2017 to December 2017 and was followed up to December 2018. Institutions ethics clearance was obtained. Informed consent was taken from parents of all study participants.

Inclusion criteria

As per diagnostic criteria of the American Academy of Pediatrics and the American College of Obstetrics and Gynecology for hypoxic-ischemic encephalopathy, 1996.⁹

Exclusion criteria

Babies diagnosed as sepsis, pathological hyper bilirubinemia, respiratory distress, intrauterine infection or trauma (i.e., skull fracture or blunt trauma of the maternal abdomen), cardiac or central nervous system malformation, chromosomal abnormality, any other congenital abnormality and/or inborn metabolic error. These babies were studied prospectively for one year. A

detailed obstetric history was recorded along with a 1-minute, 5- minute and 10- minutes APGAR score. Staging of HIE was done according to Sarnat and Sarnat criterias.¹⁰ During hospital stay babies were examined daily and managed according to standard protocol. Outcome was measured as successfully discharged or mortality at the end of hospital stay. Presence or absence of neurological sequel was assessed at one year follow up visit. Few babies were lost in follow up and taken as drop out cases. First MRI brain was done when baby was stable and any time before discharge (4 days to 28 days). Those having abnormalities in the first MRI were suggested for the second MRI and in selected cases repeat MRI brain was done after 6 months.

MRI brain was done by 0.2 tesla, open Magnatec Magnetom Concerto with gradients 20mT/m SR 40. The images were acquired with a 128 x 256 or 256 x 256 matrix, a field of view of 18 to 20 cm², and a section thickness of 4 to 5 mm. T1-weighted spin-echo (SE) images were obtained in the sagittal and axial planes. Inversion recovery images and T2-weighted SE images were obtained in the axial plane. The neonates were monitored with pulse oximetry, and a pediatrician was present throughout the examination. The average total examination time was 6070 minutes.

All relevant data were recorded in Microsoft Office excel. The results obtained were analyzed statistically in chi-square test by 'AcaStat' software.

RESULTS

Total no of babies with perinatal asphyxia was 217 during this study period. Later 156 babies were excluded according to mentioned exclusion criteria. Rest 55 babies were taken finally for the study. Out of these 55 babies, 27 were preterm and 28 were term. There were 9 (29%) babies (term 9, preterm 7) in stage I, 17 (30.9%) babies (term 8, preterm 9) in stage II and 22 (29%) babies (term 10, preterm 12) in stage III.

Multiple clinical presentations were observed in most of the cases. Lethargy (63.6%) and poor feeding (60%) were the commonest clinical presentation followed by seizures (32.7%), jitteriness (23.6%), excessive cry (21.8%) and apnea (14.5%).

MRI brain findings were normal in 8 patients (term 4, preterm 4), and rest 47 patients had abnormal findings which were documented in 4 groups according to the pattern of injury. (Table 1)

- **Group 1:** Deep gray matter injury (DG).
- **Group 2:** Para Sagittal subcortical white matter injury (PS).
- **Group 3:** Germinal matrix haemorrhage (GMH), intraventricular haemorrhage (IVH) and Periventricular leukomalacia (PVL).
- **Group 4:** Mixed pattern of injury.

Table 1: Relation of findings of MRI brain with gestational age and stages of HIE.

MRI Brain findings	Term			Preterm		
	Stage I	Stage II	Stage III	Stage I	Stage II	Stage III
DG (Group 1)	2	4	5	2	4	5
PS (Group 2)	2	3	0	0	0	1
GMH+PVWM (Group 3)	0	1	2	3	3	3
Mixed (Group 4)	0	0	3	1	1	2
Normal	4	0	0	1	2	1

DG = Deep gray matter injury, PS = Parasagittal cortical and subcortical injury, GMH = Germinal matrix haemorrhage, PVWM = Periventricular white matter injury.

Table 2: Different types of lesions in mixed injury (Group 4).

MRI brain
GMH with IVH, subarachnoid hemorrhage; lateral thalamus, posterior and medial lentiform, central cerebral white matter; T2 prolongation over entire cortex; edema in PLIC
Diffuse cortical and subcortical white matter injury, IVH
Deep gray matter injury, and extensive cortical damage and GMH
subarachnoid haemorrhage and diffuse cortical injury
Diminished hemispheric white matter; short T1 lateral lentiform, rt frontal pole; small lentiform nuclei; short T2 in lateral thalamus, posterior lentiform, rt cerebral peduncle
T1 shortening of globus pallidus, lateral putamen, lateral thalamus, T2 prolongation in entire cortex
Hypointensity in putamen and thalamus and frontoparietal white matter hyperintensity with loss of cortical ribbon

Among 7 babies who had mixed pattern of injury on MRI brain were shown in table 2.

Twenty two babies (40%) were in group 1(term 11, preterm 11), six babies (11%) in group 2 (term 5, preterm 1), twelve babies (21.8%) in group 3(term 3, preterm 9), and seven (12.7%) babies in group 4(term 3, preterm 4).

MRI brain findings among babies in HIE stage 1 were normal in 5, DG in 5, PS in 2, GMH+PVL in 3 and mixed in 1. Same for stage 2 were normal in 2, DG in 7, PS in 3, GMH+PVL in 4 and mixed in 1 and in stage 3 were normal in 1, DG in 10, PS in 1, GMH+PVL in 5 and mixed in 5. In statistical analysis, for stage of HIE with MRI findings, though 12 cells (80%) have an expected frequency less than 5, against the assumption of Chi-square. It showed $df=8$, $p <0.287$ (statistically insignificant).

When outcomes were analyzed total 9 babies were died. Among them, 4 babies (44.4%) had DG, 2 babies (22.2%) had GMH+IVH and 3 babies (33.3%) had mixed pattern of injuries in MRI.

Among 46 successfully discharged babies, 6 babies were lost to follow up. After regular follow up, at the end of 1 year, there was neurological sequel in 13 babies

(48.1%). Among them, initial MRI finding was DG in 7 babies (53.8%), PS in 1(7.7%) baby, GMH+IVH in 4 babies (30.8%) and mixed in 1 baby(7.7%).

All 7 babies who had normal MRI finding initially had no sequel. Statistically, though 6 cells (60%) have an expected frequency less than 5, against Chi-square assumption, analysis showed $df=4$ and p value <0.049 (statistically significant). (Table 3)

Table 3: Relation of MRI brain patterns with outcome.

MRI findings	Normal	Sequelae	Death	Lost follow up
DG	8	7	4	3
PS	4	1	0	1
GMH+P VL	6	4	2	0
Mixed	2	1	3	1
Normal	7	0	0	1

Repeat MRI was done in 22 babies among whom 15 babies had residual abnormalities. Initial MRI features were resolved in 4 babies with previous DG, 1 baby with previous PS and 2 babies with previous GMH+IVH injuries. Statistically, though 7 cells (87.5%) have an expected frequency less than 5, against Chi-square assumption, analysis showed $df=3$ and $p <0.552$ (insignificant). (Table 4)

Table 4: Findings on repeat MRI.

Initial MRI brain findings	Residual features	Resolved
DG	5	4
PS	2	1
GMH+PVL	5	2
Mixed	3	0
Total	15	7

DISCUSSION

In our study, term babies are distributed almost equally in three stages of asphyxia but majority of the preterm

babies were presented with features suggesting severe degree or stage III of HIE. Both the term and preterm babies had deep gray matter injury, but cortical and subcortical, parasagittal area damage were more in case of term babies. GMH, IVH and PVL were more common in preterm babies. Profound hypoxia mainly affected the deep gray matter area of brain, posterior putamen in term babies and thalamus for preterm babies. MRI brain was normal in majority of stage I and II presentation. Outcome also varied with gestational age and severity. Babies in stage II and stage III had increased mortality and morbidity. Babies with deep gray matter injury (group 1) and GMH+IVH and PVL (group 3) had increased mortality and morbidity, whereas babies with parasagittal subcortical white matter injury had good outcome.

Results of a study conducted by Barkovich and Truwit indicate that the pattern of structural damage in asphyxiated premature neonates is clearly different than that in asphyxiated term neonates.¹¹ AJ Barkovich, et al. reported four pattern of injury in babies having birth asphyxia within 10 days of life similar to our study.¹² Severity of insult affected the pattern of injury. Experiments performed in animal models have demonstrated that episodes of prolonged fetal hypoxia result in shunting of blood to vital brain structures, such as the brainstem, thalamus, basal ganglia, hippocampi, and cerebellum, at the expense of less metabolically active structures, namely, the cerebral cortex and white matter.¹³ Therefore, the brainstem, cerebellum, and deep gray matter structures are generally spared from injury in HIE I or II since auto regulatory mechanisms are able to maintain perfusion to these areas of the brain. The primary locations of ischemic injury in the term neonatal brain are the intervacular watershed zones.^{11,14} In HIE stage III, in term neonates a primarily central pattern of injury involving the deep gray matter (putamina, ventrolateral thalamus, hippocampi, dorsal brainstem, and lateral geniculate nuclei) and occasionally the perirhinal cortex was observed. These areas of the brain are actively myelinating (an energy-intensive process) or contain the highest concentrations of NMDA receptors at term and are, therefore, the most susceptible to asphyxia.^{15,16} AJ Barkovich and SK Sargent reported that MR showed T1 and T2 shortening in the thalamus in all term babies with severe hypoxia.¹⁷ In a study done by Rutherford et al. observed that infants with a normal outcome had patchy white matter abnormalities and infants with an abnormal outcome had extensive white matter abnormalities. Infants with mild HIE who are developmentally normal at the age of 2 years do not have normal MRI scans and may be at risk of minor neurological problems by school age.¹⁸ L. Liauw, et al. has studied to conclude that MRI findings are helpful to predict outcome in (near) term neonates with HIE.¹⁹ If the signal intensity in the posterolateral putamen is less than the signal intensity in the posterior limb of the internal capsule, favorable outcome is very likely, whereas if the SI in the

posterolateral putamen is equal to or greater than the SI in the posterior limb of the internal capsule, adverse outcome is very likely.¹⁹

However, the follow up study period is short and extended period of study is needed for actual detection of neurological outcome. Also, MRI is not suitable for newborn babies for whom strictly movement restriction cannot be achieved. It also has risk of hypothermia for newborn.

CONCLUSION

In spite of these short comings, with the help of MRI, correct radiological pattern of injury can be obtained and the relation of pattern of injuries with gestational age, severity of injury can be implemented in the management and prediction of future outcome of babies with HIE.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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